Remarks

I. Summary of Office Action

Applicants confirm that the Office has received and made of record the Response to Restriction Requirement filed on April 2, 2001 (Paper No. 6). Group I, claims 1 and 10 – 33, was elected without traverse and non-elected claims (34-36) have been canceled. Claims 1 and 10-33 are now pending.

In this communication, Applicants have added new claims 37 through 45. No new matter is believed to have been added with the amended or added claims. Support for the amendments to claim 10 may be found on page 9, lines 11-13; and new claims 37 through 45 can be found throughout the Specification. For example, support for independent claim 37 can be found on page 9, line 5 through page 10, line 29.

II. Claim Rejection – 35 U.S.C §112

The Office rejected claim 22 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office further indicates that claim 22 depends upon claim 21; "however, a gene is not a protein" The Office suggest that the claim 22 should depend from claim 20.

Applicants thank the Examiner for her attention to detail and for her suggestion. Applicants have amended claim 22 to properly depend from claim 20 instead of claim 21. Accordingly, this ground for rejection has been remedied and should therefore be withdrawn.

III. Claim Rejections – 35 U.S.C.§102

A. Schmitt (U.S. Patent No. 5,983,220)

The Office rejected claims 10, 12, 14 and 17-19 under 35 U.S.C.§102(e) as allegedly being anticipated by Schmitt (U.S. Patent No. 5,983,220).

The Office indicated that Schmitt "describes a computer based-database evaluation system where a user inputs desired properties of an item (thereby defining a target) and can specify the relative importance of the properties for searching a database" (Office Action page 2). The Office further indicated that the Schmitt system returns items using fuzzy logic evaluation and nearest neighbor exploration, and where the user of the system can exclude items from being identified. According to the Office, use of the Schmitt system may be used on-line using the Internet.

The Schmitt reference discusses a database evaluation system that relates to a "database technology focused entirely on the comparison and ranking of database items." (*See*, Schmitt col.2 lines 43-45). This database system requires an **authoring module** for defining a domain model having a "hierarchical set of attributes," an **evaluation engine** that creates a short list of items, a **scoring interface** which scores each item on the short list and a **proximity searcher** for displaying a nearest neighbor item.

Based upon a review of Schmitt, the first element in Schmitt refers to an authoring module for defining a domain model, which takes into consideration expert knowledge about specific application domains and subsequently maps that knowledge onto the database. Specifically, this module creates a hierarchical plurality of attributes where some attributes are further defined by other attributes, thus creating a hierarchical set of attributes. This module also provides "for weighting the attribute relative to other attributes, thereby

weighting the utility values of one attribute relative to the utility values of other attributes." (*See*, Schmitt at column 3, lines 7-10). Stated differently, Schmitt requires the ranking of attributes based upon an expert's knowledge in the field.

Based upon a review of Schmitt, it appears that the domain model is connected to an evaluation engine which allows users to access and evaluate items in the database. A user inputs a specific utility function which describes the utility for the various values of the attribute for the user. The evaluation engine then apparently selects for retrieval items of the database according to both the user defined utility function and the utility values of the selected attributes as defined in the domain model. (*See*, Schmitt at col. 3, lines 18-25). From a display with the selected items, the user is then apparently able to reduce the number of items selected or retrieved from the database. Working in conjunction with the evaluation engine, the scoring interface is understood to score the items on the user's list, further displaying for each attribute a direct manipulation mechanism. With this mechanism, the Schmitt system is understood to allow the user to alter the relative weighting of the attribute as already defined in the domain model. Lastly, Schmitt discusses a system with a proximity searcher user interface. This interface provides for nearest neighbor evaluation by displaying one of the items on the list as a reference item. The proximity searcher is understood to display a nearest neighbor item as a function of distance between reference item and the nearest neighbor item for the particular attribute.

With respect to the present claimed invention, Applicants have amended claim 10 and added new claims 37 through 45, which find support throughout the patent application as filed, specifically on page 9, line 5 through 10, line 29.

Applicants have added new claims (37-45) which relate to a computer database system and a method for organizing, associating and retrieving information where characteristics pertaining to information can be inferred from characteristics of similar information. More specifically, characteristics or parameters regarding information found in one database are similarly joined by the inference of characteristics of information located in a second database. (*See*, page 9, lines 5-9 of Specification). Such characteristics, for example, parameters of chemical compounds, can be arranged in different databases by, *e.g.,* databases housing compound toxicity, bioactivity, chemical structure, synthesis pathway, binding data, structure-activity relationship information, molecular weight, partition coefficient, price, patent coverage, and size. (*See*, page 25, lines 11-15 of Specification).

The presently claimed invention does not require ranking attributes by weighting characteristics of chemical compounds being searched, but rather, characteristics of chemical compounds can be linked to several different databases in search of desired information. The retrieval of information provided by the claimed invention is such that the information from one database is similarly joined with information of another database to create a set of data preferable to a user. A chemical similarity join is based upon a non-traditional operator (*i.e.,* an operator that evaluates the similarity of two members where 'similarity' is a composite index of some or all of the characteristics of the members being compared). Stated differently, the claimed invention focuses on a commonality or similarity among items allowing the retrieval of items that is most similar to a target item. Therefore, and unlike Schmitt, the present invention does not rank attributes nor weighs a particular

characteristic of an item relative to other characteristics to create a hierarchical set of attributes.

In order to anticipate under Section 102, Schmitt must disclose each and every element of the claimed invention. Schmitt does not disclose the joining of multiple databases to simultaneously search for items that are similar to the target item. In addition, Schmitt does not disclose to one skilled in the art to search for chemical compounds located on databases using a chemical similarity join, as claimed by the present invention. Therefore, Applicants submit that Schmitt does not anticipate the claimed invention under Section 102(e). Based upon the foregoing, Applicants respectfully request withdrawal of this rejection.

B. Cramer et al. (U.S. Patent No. 6,240,374)

The Office rejected claims 1, 10-16, 19-20, 23-29 and 33 under 35 U.S.C. §102(e) as allegedly being anticipated by Cramer et al. (U.S. Patent No. 6,240,374; herein after "Cramer").

The Office indicated that Cramer discusses searching on a database chemical compounds to select for similar compounds using a Tanimoto coefficient. The Office further indicated that Cramer discusses neighborhood properties; multiple properties; and removal criteria and other selection criteria such as price, availability, and pharmacological data. (*See*, Office Action page 3).

Cramer discusses a method for **generating** a virtual library in which all possible product molecules combinatorially derived from component parts can be searched by searching through only a combination of descriptors of the component parts comprising defining chemical transformation, reagents and cores to specify product molecules and using

molecule descriptors with neighborhood property to precalculate the characteristics of the component parts of product molecules. (*See,* Cramer at col. 10, lines 44-52). Cramer further discusses a method for searching, using the validated molecular descriptors, a virtual library for possible molecules similar to a query molecule . (*See*, Cramer at col. 10, lines 60-65).

Stated differently, Cramer describes **a method for generating** virtual libraries using validated descriptors of molecular structural diversity and searching for optimally active molecules from the virtual libraries using the validated molecular descriptors. According to Cramer, a molecular structural descriptor means "a quantitative representation of the physical and chemical properties determinative of the activity of a molecule. (*See*, Cramer at col. 14 lines 42-45).

With respect to the present invention, Applicants have amended claims 10 and added new claims 37 through 45.

The present invention discloses a computer database system retrieving information related to chemical compounds by using a chemical similarity join. More specifically, characteristics of one compound are located in one database and are joined via a fuzzy similarity join by the inference of characteristics of another compound in a second database. As set forth in the Specification, a "fuzzy similarity join" is defined as follows:

> the relationship between the retrieved information is not intuitively or organizationally related in the manner in which it is retrieved; rather this relationship is based upon the needs of a user who would otherwise be required (if possible) to laboriously search for the required data from unrelated or dispersed data sources. (*See,* page 14, lines 15-19 of Specification).

These characteristics can be located via the fuzzy similarity join in different databases by, for example, databases housing compound toxicity, bioactivity, chemical

structure, synthesis pathway, binding data, structure-activity relationship information, molecular weight, partition coefficient, price, patent coverage, and size. The present invention takes advantage of several libraries containing chemical characteristics, either locally or maintained by third parties which can be accessible to a server via a remote communication medium, and joining the characteristics contained in each library according to the needs of the user.

Cramer does not disclose the joining of at least two separate databases to create a set of data preferable to a user. Cramer at best describes a method for generating a virtual library using molecular descriptors and searching for compounds using the same descriptors within the virtual library.

Based upon the foregoing, Cramer does not disclose the joining of databases (libraries) based upon the characteristic inferences taken from several different databases to arrive at a desired data set. Accordingly, Cramer does not anticipate under section 102(e), and therefore, Applicants respectfully request withdrawal of this rejection.

C. Gerthe et al.

The Office rejected claims 1, 10-16, 20, 23-28, and 32-33 as allegedly being anticipated by Grethe et al. (hereinafter "Grethe") under 35 U.S.C. §102(b).

The Office indicated that Grethe discusses searching a chemical database to identify compounds having properties similar to a target compound. The Office further indicated that the degree of similarity can be specified by the user, which allegedly meets the limitation of providing a neighborhood range as in claim 1 of the present invention or neighborhood effect as in claims 27-28 of the present invention. (See, Office Action page 3).

Grethe discusses the calculation of a molecular similarity value for two objects based on the presence or absence of a set of 933 structural features. Grethe further discusses searches based upon a reaction similarity, and sub- and super-similarity values. Based upon a review of Grethe, a reaction similarity search uses the set of structural features to obtain a molecule component of the similarity value, and an additional set of 230 features associated with the reacting centers to obtain a 'reaction-centre' component of the similarity value. A sub-similarity is defined in Grethe as only considering those features in the query, while a super-similarity takes into consideration those features present in the candidate.

To identify a variety of potential candidates, Grethe discusses using the similarity and super-similarity searching techniques to browse through a single database containing about 65,000 commercially available compounds. Grethe further discusses using different searching techniques on the same database of compounds to find a smaller number of structurally different, active compounds.

Applicants respectfully submit that the present invention takes advantage of multiple databases and joins these databases to create a set of information requested by a user. According to the present invention, the joining of multiple databases via a fuzzy similarity join is based upon an inference of characteristics from differing databases. This inference is, in the case of a chemical fuzzy similarity join, a composite index of the chemical similarity between chemical compounds. As indicated above, Grethe utilizes a single database to search and narrow for chemical compounds of interest. Grethe notes, "Intersection of the hit lists provides a small number of structurally different, active compounds...Additional important information is gained by a sub-similarity search over the same database." (*See*, Grethe at page 404). The presently claimed invention eliminates the need for taking the

results from one search and applying that data to search again on the same database, however, with different searching techniques, in hopes of narrowing the number of candidate compounds. Instead, the present invention allows a preferred user to simultaneously search various databases to retrieve a chemical compound most similar to the target compound, this via the fuzzy similarity join.

Based upon the foregoing, Gerthe does not disclose the joining of multiple databases to create a set of information based upon the chemical similarity among compounds. Indeed, Gerthe does not anticipate the claimed invention. Therefore, Applicants respectfully request withdrawal of this rejection.

IV. Claim Rejections – 35 U.S.C §103

A. Claims 23-24 and 30-31 Are Rejected under Section 103(a)

Claims 23-24 and 30-31 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over either Grethe or Cramer (U.S. Patent No. 6,204,374) in view of Schmitt (U.S. Patent No. 5,983,220).

The Office indicated that Grethe, applied as above, performs the method on a main frame. The Office points out that Grethe does not disclose remote communication links or the Internet.

The Office indicated that Cramer, applied as above, does not disclose remote communication links or the Internet.

The Office further indicated that Schmitt is relied upon only to establish that those of skill in the art would have routinely been aware of the ability to perform database searches via the Internet and the desirability of doing so.

Therefore, the Office concluded that "it would have been obvious to perform the method of Grethe or Cramer using the Internet to access the desired databases or computer software or communicate the results of a search to a user."

Applicants respectfully disagree and traverse.

A. Grethe in view of Schmitt

For a reference to obviate a claimed invention (alone or in combination) the reference(s) must motivate or suggest one skilled in the art to combine the references. Gerthe discusses the calculation of a similarity value and searching on a main frame using these values. Gerthe does not suggest one skilled in the art of retrieving candidate compounds to search on the Internet and similarly join data from multiple databases to create a set of information according to the user. Instead, Gerthe discusses conducting an initial search using the similarity and super-similarity techniques to browse through **a single** database holding 65,000 chemicals and subsequently conducting another search with different searching techniques on the **same** database as a method of narrowing the possible chemical candidates.

Based upon the foregoing, Gerthe provides no motivation or suggestion to combine the searching techniques of Gerthe with the use of the Internet, as discussed in Schmitt. Instead, Gerthe teaches away from using the Internet because Gerthe reports the use of different searching techniques within the **same** mainframe database to identify compounds with similar properties. Therefore, Applicants respectfully request withdrawal of this rejection.

B. Cramer in view of Schmitt

The Office indicated that Cramer discusses searching a database of compounds to select for compounds similar to a target compound and that one skilled in the art of chemical searching would have routinely been aware of the ability to perform database searches via the Internet, as discussed in Schmitt. Therefore, the Office indicated that it would have been obvious to use the method of the Cramer patent using the Internet to access the desired databases.

Applicants respectfully submit that neither Cramer nor Schmitt suggests a computer database system which uses a chemical similarity join as a method to join data from one database with that of another to retrieve a chemical compound similar to the target compound where the method of retrieving such information is on a remote communication link or the Internet.

As mentioned above, Cramer discusses the generation of virtual libraries and searching for optimally active molecules from the virtual libraries using validated molecular descriptors. There is no motivation or suggestion to combine the virtual libraries as discussed in Cramer with any remote communication links such as the Internet, of the Schmitt patent. Therefore, it would not have been obvious to have a computer-database system wherein various databases located on remote communication links are joined together to create a data set of information (*e.g*, a chemical compound similar to the target compound) preferable to a user. Applicants respectfully request that this ground for rejection should also be withdrawn.

IV. Claim Rejections – 35 U.S.C. §103

Claims 10 and 20-22 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schmitt.

The Office indicated that Schmitt, applied as above, is directed to searching any type of database. The Office further indicated that,

> Schmitt does not specifically disclose biological compound databases such as protein or gene databases. However, such databases would have been known in the art (for example SwissProt for proteins and GenBank for genes) and routinely searched for proteins or genes structurally similar to a target sequence. (*See*, Office Action page 4).

Therefore, the Office concluded that it would have been obvious to search known databases using the general methodology of Schmitt. Applicants respectfully disagree and traverse.

As mentioned above, Schmitt discusses a database evaluation system that relates to a "database technology focused entirely on the comparison and ranking of database items." (*See*, Schmitt col. 2, lines 43-45). Schmitt provides for weighting attributes (*i.e.*, designating utility values on an attribute) relative to other attributes and thus creating a hierarchical set of attributes. Schmitt does not disclose a computer-database system for retrieving information where the characteristics of a chemical compound located on a database is joined with similar characteristics of another compound located on a separate database, much less, as the Office correctly indicated, a "biological compound databases such as proteins or gene databases." (*See*, Office Action at page 4). Stated differently, Schmitt does not render claims 10 and 20-22 obvious. To do so, there must be some reason, other than hindsight, obtained from the present invention itself. The present invention must be viewed not with the benefit of having first read Applicant's specification but in the state of the art that existed at the time of the invention. Based upon Schmitt, no suggestion exists

that one skilled in the art would have possessed a reasonable expectation of succeeding in the endeavor of generating computer-database system combining information based upon inferences taken from separate databases such as from a biological database. Therefore, it is respectfully requested and is deemed proper that the §103 rejection of claims 10 and 20-22 over Schmitt be withdrawn for the reasons mentioned.

V. Conclusion

Claims 1, 10, 23 and new claim 37 are independent claims. Claims 11 through 22, inclusive, are dependent upon claim 10, or claims dependent upon claims 10. Claims 24 through 33, inclusive, are dependent upon claim 23, or claims dependent upon claim 23. Claims 38 through 45, inclusive, are dependent upon claim 37, or claims dependent upon claim 37. Previously, on April 28, 1999, Applicants (a small entity) paid the basic filing fee of $380; in the application as filed, there was one independent claim, and 9 total claims. With the preliminary amendment, filed on April 25, 2000, there were four (4) independent claims, *i.e.,* one extra independent claim, and 27 claims total, *i.e.,* 7 extra claims (there are no multiple dependent claims). Based upon those extra claims, Applicants submitted a check in the amount of $192 to cover the cost of the extra claims. It is believed that Applicants miscalculated the claim fees and overpaid by ninety dollars ($90). Instead, a check in the amount of $102 for seven (7) extra claims and for one (1) additional independent claim should have been submitted thereto.

With the current amendment, Applicants added one (1) independent claim (for a total of 4 independent claims), and eight (8) dependent claims (for a total of 30 dependent claims). Based upon the amendments in this response and what Applicants believe to be an overpayment in our April 25, 2000 response, no additional fee is believed to be required.

However, if this in incorrect, Applicants authorize the Office to charge any deficiencies to Deposit Account No. 50-1441.

For the foregoing reasons, it is respectfully submitted that the rejections set forth in the outstanding Office Action are inapplicable to the present claims. Accordingly, Applicants request that amended claim 10 and 22 and new claims 37 through 45 and all claims remaining in the Application which depend therefrom be allowed, and an issuance of Notice of Allowance be earnestly solicited.

The undersigned has made a good faith effort to respond to all the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to contact the undersigned.

Respectfully submitted,

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Ann A. Nguyen
Attorney for Applicants
U.S.P.T.O Reg. No. 46,087

Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, CA 92121
858.453.7200 x294 (phone)
858.677.0065 (fax)

Attachments:

"Version with markings to show changes made"

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 10(Amended) A computer-based method for [identifying, from a database] retrieving information that is based upon at least one similarity among entities in one or more databases, comprising items[,] with at least one item having [a] at least one property similar to a target item, the method comprising:

identifying a target item; and

using a computer to perform a fuzzy similarity join on the database to retrieve at least one item from the database that comprises at least one property similar to a property of the target item.

Claim 22 (Amended) A method according to claim [21] 20 wherein the target item is a gene.

--Claim 37 A computer database system for organizing, associating and retrieving information where characteristics regarding entities can be inferred from the characteristics of similar entities, having at least two sets of information located on one or more databases comprising a first and a second collection of information, wherein the first collection of information is joined with the second collection of information to create a set of joined items, wherein the items are grouped together based on a plurality of properties.--

--Claim 38 The system of claim 37 wherein the information is joined by a chemical similarity join.--

--Claim 39 The system of claim 38 wherein one or more properties of the plurality of properties is selected from the group consisting of chemical structure, synthesis pathway, binding data, biological activity, structure-activity relationship information, molecular weight, partition coefficient, electric charge, size, efficacy, toxicology, manufacturer, price, and availability.--

--Claim 40 The system of claim 37 wherein the resultant joined items are reported to a user of the computer program.--

--Claim 41 The system of claim 40 wherein the user interacts with the joined items via remote communication link.--

--Claim 42 The system of claim 41 wherein the remote communication link is the Internet.--

--Claim 43 The system of claim 37 wherein the entities are biological compounds.--

--Claim 44 The system of claim 43 wherein the biological compounds are proteins.--

-- Claim 45 The system of claim 37 wherein the entities are genes.--